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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S): Sham N. Redkar et al.
SERIAL NO. : 10/826,538
FILED : April 16, 2004
Examiner: Victor Taylor Oh
Art Unit: 1625

FOR: HOT MELT METHOD FOR PREPARING DIPHENHYDRAMINE TANNATE

DECLARATION UNDER 37 C.F.R. § 1.132

I, VILAS M. CHOPDEKAR, hereby declare and say that:

I am a co-inventor of the invention described and claimed in the above-identified patent application;

I am the technical director and the senior vice president of the assignee;

I hold the M.S. degree in organic chemistry granted by the University of Bombay in 1964 and the M. tech degree granted by the Indian Institute of Technology of Kharagpur, India in 1965;

I have over 39 years of experience as a research chemist;

I am a named inventor in 22 issued U.S. patents and 3 pending U.S. patent applications;

I have carefully reviewed the Office Action mailed June 2, 2004 in which the Examiner has finally rejected the claims on the basis of Chopdekar et al. (US Patent 5,663,415 hereinafter referred to as the '415 patent) in view of Gordziel (US Patent 6,287,597) and Sikora et al. (US Patent 6,268,012).

I am fully familiar with the freeze-dry process disclosed and claimed in the '415 patent since I am the first-named co-inventor in that patent;

In the '415 patent, diphenhydramine tannate is prepared by reacting diphenhydramine free base in the presence of water (50 wt.%) at a reaction temperature of 65 to 70°C for a period of 5 minutes to 4 hours, and thereafter recovering the product diphenhydramine tannate from the reaction mixture by subjecting the reaction mixture to freeze-drying at a pressure of not greater than 500 milliTorr and a temperature in the range of about –60 to about -20°C;

I attempted to recover diphenhydramine tannate from the reaction mixture by the typical solvent evaporation method conducted under vacuum and moderate temperatures, but I was not successful in respect to such method, as witnessed from the following experiment:

In this experiment, 30g of purified water, was placed in a reaction vessel and the water was heated to 70°C. Thereafter, 17g (0.01 mole) of tannic acid were added, while stirring, over a period of 15 minutes, while maintaining a temperature of 70°C. Then 12.75g (0.05 mole) of diphenhydramine base were added, with stirring, over a period of 5 minutes, while maintaining the temperature at 70°C. The reaction mixture was stirred for an additional 30 minutes, while maintaining the temperature at 70°C. The resultant thick reaction mixture was then poured into a glass tray that was placed in a vacuum oven and 50 mm Hg of vacuum was applied. The temperature of the oven was slowly raised to 80°C. It was noted that the entire mass started rising like a balloon and touched the sides and the top of the vacuum oven. The vacuum was broke after 2 hours and the bubble deflated after a few minutes. Vacuum was again applied and the temperature was held at 80°C and again a bubble was formed that filled the chamber of the oven. The experiment was stopped after 4 hours. The product was obtained in 73% yield free of water . It was noted that the vacuum oven had a lot of semisolid product adhering to the walls of the oven and some product also went into the vacuum line. This experiment showed that it was not practicable to remove the free water from the reaction product by evaporation of the water from the reaction mixture.

A comparison was made between the process parameters and the processing cost, measured.

in $/kg, between 30 kg batches of diphenhydramine tannate prepared by the hot-melt process disclosed and claimed in the instant application and the freeze-dry process disclosed and claimed in the '415 patent. The results of such comparison are as follows:

	Hot-Melt Process	Freeze-Dry Process
Reaction Time	2 hours	2 hours
Reaction Temp., °C	85-90	65-70
Free Water, wt.%	10	50
Drying Time, hours	8	108
Total Processing Cost, $/kg	23.89	194.67

From the results set forth above, it is clear that the product cannot be recovered from the reaction mixture by conventional vacuum drying when the reaction is carried out at temperatures of 70°C or below in the presence of 50 wt.% free water (as disclosed in the '415 patent). It is also clear that the hot-melt process of the instant invention is unexpectedly superior to the freeze-dry process of the '415 patent both in terms of process time as well as process cost.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

July 6, 2005
Date

Vilas M. Chopdekar